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Inhibition of bile salt-induced gastric mucosal erosions by 16,16 dimethyl prostaglandin E_2 in the rat

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Exposure of the rat gastric mucosa to bile salt (sodium taurocholate, ST) and concurrent administration of indomethacin may lead to erosion formation. Such erosions can be inhibited by prostaglandins even in the presence of exogenous acid (Whittle, 1976) suggesting that prostaglandins have a protective effect on the mucosa, in addition to their anti-secretory actions.

We have investigated the effects of 16,16 dimethyl PGE_2 (MePG) on erosions induced by ST alone using the rat gastric chamber preparation (Mersereau & Hinchey, 1973). The mucosal solution (10–100 mM HCl made iso-osmotic with mannitol) was replaced every 0.5 h and H^+ loss, Na^+ gain and mucosal blood flow (MBF) (aniline clearance, Main & Whittle, 1973) were measured.

Erosion formation was related to the concentration of ST (present for one 0.5 h period) and acid (present from 2 h before until 2 h after ST). The erosion indices 1.5 h after exposure to 20 mM ST in 10 mM HCl (3 ± 2.5, $n=3$) or 2 mM ST in 100 mM HCl (0, 12, $n=2$) were not significantly different from controls (0 and 5.5 ± 5, for 10 and 100 mM HCl respectively, $n=4$).

With 5 mM ST (100 mM HCl) erosion formation began during the exposure period, rose rapidly in the next period and continued to rise for the remaining 1.5 h of the experiment. H^+ loss (per 0.5 h period) increased from 39 ± 11 to 99 ± 7 μmol ($P<0.05$, $n=4$) during ST then fell steadily. Na^+ gain increased from 26.6 ± 4 to 39.8 ± 4 μmol ($P<0.01$) during ST, reached a maximum (65.5 ± 5 μmol, $P<0.01$) in the next period then declined. MBF was unchanged during ST but rose rapidly in the next period ($237 \pm 9\%$ of basal, $P<0.001$) and remained significantly elevated.

MePG (15 μg ml) in contact with the mucosa from 0.5 h before until 1 h after ST (5 mM, 100 mM HCl) inhibited erosion formation (index reduced from 44 ± 9 to 6 ± 3, at 1.5 h $P<0.01$, $n=4$) while a lower concentration (5 μg ml) had no significant effect (32 ± 11, $n=4$).

Although no H^+ loss was noted with the low concentration of MePG prior to ST there was an increased loss (35 ± 4 to 59.5 ± 9 μmol, $P<0.05$) with the high concentration. However, this latter concentration reduced the increased loss due to ST (from 99 ± 7 to 63 ± 15 μmol, $P<0.05$). Na^+ gain increased from 17 ± 4 to 43 ± 5 μmol ($P<0.01$) and 17.2 ± 2 to 36.7 ± 5 μmol ($P<0.01$) for high and low concentrations respectively during the first period of MePG application but did not increase further during ST. MePG raised MBF to $142 \pm 9\%$ ($P<0.01$) and $130 \pm 4\%$ ($P<0.001$) for high and low concentrations respectively but failed to affect the further rise following ST.

These results show that MePG applied topically can protect the mucosa against ST. This protective action was associated with a reduction in the increased mucosal permeability to H^+ caused by ST. Protection is unlikely to result from the marked effects on Na^+ transport or MBF since both concentrations of MePG studied had similar effects on these parameters though the lower concentration did not prevent erosions.

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